



Hyperthyroid Heart Disease with Some Comorbidities

Abdi Dzul Ikram Hasanuddin^{1*}, Sandra Dunggio², Hannan Zubaidi²

¹Bachelor Program of Medicine, State University of Gorontalo, Indonesia

²RSUD Otanaha, Gorontalo, Indonesia

Corresponding author () e-mail: abdidzulikram@gmail.com

Phone number: +6285233215280

Received 5 March 2020; Accepted 30 March 2020; Published 4 April 2020

ABSTRACT

Thyroid disease is quite common. The cardiovascular clinical manifestations of hyperthyroidism are palpitation, systolic hypertension, fatigue, or with the basis of existing heart disease, angina or heart failure. In men, the disease is more frequently to develop into congestive heart failure than in women, thus more exploration is needed. This case report discussed a 42-year-old male patient who was admitted to the emergency department due to palpitations, shortness of breath aggravated with activity and lie down position, and alleviated with resting, cough with white sputum, epigastric pain, and constipation since the past 3 days. He was diagnosed with a history of hyperthyroidism and congestive heart disease 1 year ago and routinely consumed propylthiouracil (PTU). He had a history of herniotomy 10 days before admission. The patient did not have a history of hypertension, diabetes mellitus, or hypercholesterolemia. The patient has a smoking habit of up to 3 packs daily since a teenager. The patient was diagnosed with hyperthyroid heart disease (congestive heart failure, atrial fibrillation, and coronary heart disease) with comorbid of electrolyte imbalance, hypoalbuminemia, and thrombocytopenia. The patient was treated in the Intensive Care Unit (ICU) and was given oxygen therapy, crystalloid infusion, anti-thyroid drug, beta-blocker, diuretics, digitalis, anti-angina, anti-thrombotic, and adjunct therapy. The patient was treated for 8 days in ICU, followed by 2 days in the ward with a good outcome. Early detection and intervention followed by close monitoring is key management for the patient with hyperthyroid heart disease, especially in a male patient, to achieve a better outcome.

Keywords: Atrial fibrillation; congestive heart failure; coronary heart disease; hyperthyroidism; hypoalbuminemia

Introduction

Thyroid disease is quite common. Current data estimate 9% to 15% of the adult female population and smaller presentation in the adult male population with this disease. Prevalence occurs because of the autoimmune effects that underlie the onset of this disease, such as Grave's disease and Hashimoto's disease. Nonetheless, as this disease is a gender-specific, but with increasing age, the prevalence between male and female sex are equal.¹

The cardiovascular clinical manifestations of hyperthyroidism are palpitation, systolic hypertension, fatigue, or with the existing heart disease, angina or heart failure. Sinus tachycardia is found in 40% of patients and 15% with atrial fibrillation in hyperthyroid patients.²

In elderly patients with hyperthyroidism, called apatetic hyperthyroidism, thyrotoxicosis can only be seen in cardiovascular manifestations, including atrial fibrillation, and may be resistant to therapy until the condition of hyperthyroidism is controlled. Angina pectoris and congestive heart failure are rare unless they are related to the existing heart disease and many cases of symptoms diminish after the hyperthyroidism is resolved.² We present a case of hyperthyroid heart disease (congestive heart failure, atrial fibrillation, and coronary heart disease) with comorbid of electrolyte imbalance, hypoalbuminemia, and thrombocytopenia. This case underlines the importance of early detection and intervention followed by close monitoring in patient with hyperthyroid heart disease.

Case

A 42-years-old male, was admitted to hospital upon complaining of palpitations for the last 2 days. He had shortness of breath aggravated with activity and lie down position, and alleviated with resting since 2 days ago. He also reported stomachache, distended abdomen, and bloating for the last 3 days. The complaint was accompanied by constipation and unable to pass gas for the past 2 days. Pain in the pit of his stomach was also reported for the past 3 days. The patient also complained of coughing, occasionally accompanied by white sputum.

The patient had a history of similar complaint 1 year ago and been diagnosed with hyperthyroidism. Since then, he routinely consumed PTU medication every day. When diagnosed as having hyperthyroid 1 year previously, he was found to already have a swollen heart. Patient had a hernia that he have been felt since December 2015 and undergone surgery in Aloe Saboe Hospital 10 days previously. The patient did not have a history of hypertension, diabetes mellitus or hypercholesterolemia. Likewise, there was no hypertension, diabetes mellitus, hypercholesterolemia, goiter, or heart disease in the patient's family. The patient had a marital problem, and was in divorce process since 1 year previously. Patient also have a smoking habit up to 3 packs/day since teenager.

In the emergency department, the blood pressure was 130/80 mmHg, the pulse rate was 80 times per minute irregular, breathing was 24 times per minute, body temperature was 35.5⁰C and oxygen saturation was 98%. The patient appears to be moderately ill but was still conscious. There was no cyanosis, anemia, or jaundice on physical examination. Exophthalmus in both eyes were found and there was an increase of jugular venous pressure. No enlargement of the thyroid gland was found. On examination, the lungs were found within normal limits, while there was irregular heart I/II sounds accompanied by gallop S3. On examination, the abdomen appeared distended, there was a scar of surgical incision on the lower right abdomen, increased bowel sounds, epigastric tenderness, and unpalpable of the liver and spleen. In the extremities, pitting edema was found but the acral was still warm.

On routine blood tests obtained in the emergency department, Hb 13.4 g% (reference value 11.0 - 16.5 gr%), Leukocytes 4,600/mcl (reference value 3,500-10,000/mcl), Platelet 91,000/mcl (reference value 150,000-390,000/mcl), and Hematocrit 30.4% (reference value 35-50%). On kidney function, liver function, lipid profile, and electrolyte serum tests obtained on emergency department, Ureum 14 mg/dl (reference value 10-50 mg/dl), Creatinine 0.71 mg / dl (reference value 0.7 - 1.5 mg/dl), SGOT 37 U/L (reference value 11-41 U/L) and SGPT 31 U/L (reference value 10-41 U/L), Total Cholesterol 106 mg/dl (reference value 140-199 mg/dl), LDL Cholesterol 76 mg/dl (reference value <130 mg/dl), and HDL Cholesterol 25 mg/dl (reference value L:35-65 mg/dl P:35-80 mg/dl), Sodium 131.2 mmol/L (reference value 135-145 mmol/L), Potassium 4.26 mmol/L (reference value 3.5 - 5.0 mmol/L), and Chloride 106,9 mmol/L (reference value 98-106 mmol/L). On initial ECG in the emergency department, we found Atrial Fibrillation Normo Ventricular Response HR 80x/minutes, Left Ventricular Hypertrophy, and Normoaxis. The patient was diagnosed in the emergency department with Hyperthyroid Heart Disease (Atrial Fibrillation Normo Ventricular Response HR 80x/minutes and Congestive Heart Failure), Hyperthyroid on treatment (PTU), Imbalance Electrolyte, and Thrombocytopenia. Patient was decided to get closely monitoring in Intensive Care Unit (ICU).

During treatment in the ICU, the patient had clinically improved condition where on day 5, symptoms significantly decrease. Based on several hematology test (day 2 and day 3), thrombocytopenia still persist with value 113,000 and 91,000,

respectively but without signs of bleeding. The electrolyte level on day 3 is still abnormal, with mild hyponatremia (Na 131,2 mmol/L) but was corrected into the normal limit on day 6 (Na 142 mmol/L) without any specific treatment. For sharpen the diagnosis, we performed protein and albumin level tests (on 4th-day care), and urinalysis (on 5th-day care). On examination of protein level tests, it revealed total protein 4.9 g/dl (reference value 6.2 -8.4 g/dl) and Albumin 2.4 g/dl (reference value 3.5-5.5 g/dl). From urinalysis, proteinuria was not found. Examination of thyroid hormone function cannot be conducted due to lack of resources.

During treatment in the ICU, serial electrocardiography (ECG) monitoring was performed and various abnormalities were found (Table 1). Moreover, we performed imaging examination on day 5 to help establish the diagnosis (Figure 1). Chest X-ray examination in postero-anterior position found cardiomegaly with cardiogenic acute lung oedem (ALO) signs, accompanied by bilateral pleural effusion. Whereas the abdomen ultrasonography (USG) examination was found hepatomegaly with signs of liver congestion. No free fluid was found in the peritoneal cavity. Finally, the patient was diagnosed with hyperthyroid heart disease (congestive heart failure, atrial fibrillation, and coronary heart disease) with comorbid of electrolyte imbalance, hypoalbuminemia, and thrombocytopenia.

The patient was treated in ICU for 8 days, followed by 2 days in ward with good outcome. The given treatment were oxygen therapy, crystalloid infusion, anti-thyroid drug, beta-blockers, diuretics, digitalis, anti-angina, anti-thrombotic and adjunctive agent. Summary of daily follow up and detailed treatment given is shown in Table 2.

Discussion

Patient was a 42 years old male. Based on the literature, the prevalence of hyperthyroidism is more common in middle age while women are more frequent than men with a ratio of 1: 5.¹ This is a rare case, but in men is more frequent to develop into congestive heart failure than in women, so we must give more attention in this situation.²

Patient present with a major complaint of chest palpitations since the last 2 days accompanied by shortness of breath. Patients had a history of being diagnosed with hyperthyroidism 1 year ago and routinely consumed PTU drugs. This is a typical complaint in hyperthyroidism disorders and often makes patients come to see a doctor.³

The patient also complained that his stomach feels bloated in the past 3 days and felt enlarged, which has made the patient felt uncomfortable. The patient also couldn't defecate and passing gas in 2 days. Patient also complained of heartburn in the past 3 days. These were non-specific complaints in patient who initially present with hyperthyroidism.

Patient also complained of coughing, occasionally, accompanied by white sputum in the past 3 days. This is not a typical complaint in hyperthyroidism, but can be a sign of heart failure.⁴

On the psychosocial aspect, the patient was currently having a marriage problem and undergoing divorce process in court since 1 year previously. Patient also have smoking habits up to 3 packs/day since he was a teenager. It is suspected that this habit aggravate the patient's hyperthyroidism condition, especially complications of heart failure abnormalities.⁵

From initial vital signs in emergency department, there were two data that support the diagnosis of hyperthyroidism, the first data was irregular heart beat and the second data was rapid breathing, up to 24 x/minutes. From head to toe physical examination found a positive exophthalmus (+/+), increased JVP, normal lung examination, irregular heart rhythm accompanied by gallop sound S3, pitting edema in all the extremities showed a typical hyperthyroidism with complications of hyperthyroid heart disease (atrial fibrillation and congestive heart failure).^{4,6}

From the abdominal examination it was shown that the abdomen appeared distended, there was a scar of surgical incision on the lower right abdomen (from hernia surgery 10 days previously at other regional hospital), increased bowel sound, epigastric tenderness, and unpalpable of the liver and spleen. These were not specific finding of hyperthyroidism condition, but rather leads to the diagnosis of ileus and dyspepsia syndrome. After several days of follow-up, it was thought that the cause of abdominal abnormalities was ascites, on the basis of positive shifting dullness on physical examination, accompanied by laboratory results of hypoalbuminemia and hypoproteinemia. Although abdominal ultrasound examination was found no free fluid in the peritoneal cavity, but there was hepatomegaly with hepatic congestive signs, and bilateral pleural effusion. Related to the main disease of the patient, hyperthyroidism,

these were in accordance with complications of congestive heart failure, experienced by the patient.⁴

Routine blood tests showed thrombocytopenia that still persists until on the 3rd-day care. This was probably due to the side effect of long term use of PTU, as has been reported in a study and a case report.⁷ However, the patient's condition was different from that reported in the study because there were no signs of bleeding in this patient.

Examination of kidney function (urea, creatinine) and liver function (SGOT, SGPT) was within normal limits. This was in accordance with the condition of hyperthyroidism, and eliminates other possible diagnoses such as hepatic cirrhosis and chronic kidney failure which can also provide complaints and similar physical examination findings. Examination of lipid profiles was found a decrease HDL, which supports hyperthyroidism in the patient.⁸

Examinations of albumin and serum protein were found hypoalbuminemia and hypoproteinemia. The result of urine examination was found no proteinuria. This is in accordance with the condition of hyperthyroidism and eliminates other possible diagnoses such as liver cirrhosis and chronic kidney failure which can also provide a similar picture of laboratory results. Serum electrolyte examination showed a sign of electrolyte imbalance in the form of hyponatremia and hyperchloremia, which is not typical in patients with hyperthyroidism. The patient was not tested for thyroid hormones, neither TSH, free T₄, nor T₃, due to cost constraints and the hospital availability of such examination. Based on recent guideline, it is very recommended to perform thyroid testing for management of thyroid dysfunction coexistent with cardiovascular disease, especially for patient that have atrial fibrillation and heart failure as like as our patient condition.⁹

Serial ECG examinations showed various abnormalities, including atrial fibrillation, PVC/VES, T wave inversion, and signs of LVH. Atrial fibrillation is a disorder that is commonly found in hyperthyroid heart disease patients.⁴ PVC/VES is a disorder that is rarely found in cases of hyperthyroidism, except if the patient already has an underlying heart abnormality. There is a possibility of underlying Coronary Heart Disease (CHD), because the ECG picture showed a T wave inversion.¹ According to Sokolow-Lyon voltage criteria, LVH is a total S wave at V₂ and R wave in wave V₅ > 35 mm, and this result supports the patient's diagnosis of congestive heart failure.¹⁰

PA Thorax X-ray showed cardiomegaly and acute lung edema signs, accompanied by bilateral pleural effusion. This supports congestive heart failure as the cardiovascular complications in this hyperthyroid patient. Hepatomegaly and congestive signs of the liver was found from abdomen ultrasound examination. Hepatomegaly due to hepatic congestion are a sign of high output heart failure in hyperthyroid heart disease. This supports the picture of congestive heart failure as a cardiovascular complication in this hyperthyroid patient.⁵

To determine the diagnosis of this patient, the diagnostic criteria for hyperthyroidism and hyperthyroid heart disease must be met. Hyperthyroidism in these patients is based on history, physical examination, and laboratory and radiology investigation. The gold standard is the examination of thyroid hormones levels, namely TSH levels, free T4, and T3. Unfortunately, in this patient it could not be done. Data that helps establish a diagnosis of hyperthyroidism in these patients are palpitations, history of diagnosis of hyperthyroidism in the past year and routine consumption of PTU, irregular pulse and heartbeat, exophthalmus oculi and atrial fibrillation.

Atrial fibrillation was established based on complaints of palpitations accompanied by ECG images, which shown P waves of fibrillation and irregular distance of R-R. Coronary Heart Disease was established based on ECG results that showed a unifocal PVC image and in the T wave host house in lead V4-V6. The diagnosis of congestive heart failure was made based on the Framingham criteria⁶, which found 5 major criteria (neck venous distension, elevation of jugular venous pressure, cardiomegaly, acute pulmonary edema and S3 gallop) and 3 minor criteria (extremity edema, hepatomegaly, and pleural effusion). This fulfills the diagnostic criteria where at least 1 major criterion is found with 2 minor criteria.⁶

During treatment at the hospital, this patient get medical and non-medical therapy. Non-medical therapy include total rest, heart diet that aim to reduce the burden of the heart with a soft, low salt, low calories, and high protein diet, and reduce all forms of stress both physically and psychologically which can aggravate the work of the heart.

Medical therapy includes oxygen, supportive IV fluid, antithyroid drugs, beta blockers, diuretics, digitalis, anti-coagulants, and anti-angina. Two liter per minute nasal canal O₂ was given as a supplementation therapy to help increase oxygen supply into the

lungs and thus reduce complaints of dyspnea in this patient. Supportive fluids, namely Ringer Lactate 18 drops per minute, was given to maintain hemodynamic and fluid balance in this patient. Given the condition of fluid overload in this patient, the amount of fluid through the infusion is limited to about 1200-1300 cc/24 hours.

100 mg of PTU tablets every 8 hours was the chosen antithyroid drug in hyperthyroidism. PTU has the work of inhibiting T4 changes to peripheral T3, so that PTU shows symptomatic treatment faster, most patients can be controlled for hyperthyroidism with 100-150 mg of PTU every 6-8 hours.^{6,12} However, from other literature, the appropriate dose for patient with Hyperthyroid disease is PTU 250 mg or 400-600 mg/day. The dosage three times a day from PTU is reduced to 200 mg after about 2 weeks (tapering off), then gradually reduced to 100 mg after about 8 weeks. Subsequently the maintenance dose can be given 50 mg three times a day or approximately 1-1.5 year.¹¹ In the administration of PTU, since the patient shows a different response, the dose must be monitored with plasma T4 and T3 levels. The time needed for plasma T4 and T3 to return to normal varies around 6-10 weeks.⁶ However, in these patients T4 and T3 serum levels were not monitored due to constraints to our hospital availability. They are guide us when to start and adjusting the antithyroid drug dosage during treatment, particularly if the patient have ventricular rate that is difficult to control with standard treatment.⁹

20 mg of propranolol tablets per 8 hours is the drug of choice in hyperthyroidism, with recommended doses of 40-160 mg tablets/day in divided doses. This drug is a beta blocker class which is intended to reduce the work of the heart and fight the work of negative inotropic and chronotropic thyroid hormones. Propranolol will rest the heart and give longer diastolic filling time so that it will overcome the heart failure. Propranolol is also important to overcome the peripheral effects of thyroid hormones which stimulates beta-adrenergic receptors. Beta blockers are also suppressing the nervous system, which can reduce palpitations, anxiety, and hyperkinesis. Provision of propranolol can be stopped if therapy with PTU has shown good results.¹³ In this patient the administration of propranolol was stopped at 5th-day care, because there was a clinical improvement response in patient after being given PTU medication. Bisoprolol 2.5 mg tablets per day is a beta blocker class of drugs given to patients when there are abnormalities of heart failure. The initial dose is 1/10 of the

target dose, gradually 2x titrated according to the patient's clinical response. The mechanism of action is similar to propranolol, only this drug works for a longer duration.¹¹

Furosemide IV injection 20 mg per 12 hours is a strong diuretic as the treatment of choice for patients who have heart failure. Administration of this drug is intended to reduce congestive signs and symptoms. Especially in this patient where fluid overload and high-output heart failure occurs. The initial dose given was 2x20 mg intravenously (40 mg daily dose) in 2 days of treatment, and it was greatly reducing the patient's congestive complaints. After that, Furosemide tab 10 mg was continued in the morning for maintenance.¹²

Spirolactone 50 mg tablets per 8 hours is an aldosterone antagonist that works by carrying out competitive inhibition of aldosterone downstream of the distal tubule and the ducts of the colon in the renal cortex. In chronic heart failure, administration of spironolactone is intended to prevent myocardial remodeling. This drug is given with Furosemide to increase the diuresis effect and prevent hypokalemia. Adult doses range from 25-200 mg, but effective doses a day are on average 100 mg in single or divided doses. After 1 week of treatment, the dose of the drug spironolactone in this patient is reduced to the lowest daily dose, which is 25 mg once a day, every morning.⁹ Spirolactone 50 mg tablets per 8 hours is an aldosterone antagonist that works by carrying out competitive inhibition of aldosterone downstream of the distal tubule and the ducts of the colon in the renal cortex. In chronic heart failure, administration of spironolactone is intended to prevent myocardial remodelling. This drug was given with Furosemide to increase the diuresis effect and prevent hypokalemia. Adult doses range from 25-200 mg, but effective doses on average are 100 mg a day in single or divided doses.¹² After 1 week of treatment, the dose of spironolactone in this patient was reduced to the lowest daily dose, which was 25 mg once a day, every morning.

Digoxin 0.125 mg tablets per 12 hours is still controversial, because of its negative chronotropic nature but positive inotropic. It is expected that the negative chronotropic will work to overcome the existing tachycardia, but the positive inotropic work can increase the work of the heart.¹² However, in this patient heart failure is accompanied by atrial fibrillation which has received maximum therapy with beta-blockers for 1 week of treatment. This was an indication of the use of digitalis in this

patient. The dose of digoxin is usually 0.125-0.25 mg a day in normal kidney function (in the elderly 0.0625 mg-0.125 mg, sometimes 0.25 mg).⁶

Thromboaspilet 80 mg tablets per day is an anticoagulant recommended for cases of atrial fibrillation in young patients, without organic cardiac abnormalities, hypertension, or other independent risk factors that can cause embolism. Treatment with anticoagulants, especially if the condition returning to the sinus rhythm and euthyroid in 3 days or more, is continued for 4 weeks later. Aspirin as antithrombotic has an effective dose of 80-320 mg per day.¹¹

ISDN 5 mg tablets per 12 hours is a group of nitrates commonly used in patients with complaints of angina. In these patients, a picture of unifocal PVC and lead V2-V4 T wave inversion was found which showed the presence of coronary heart disease. In addition, patients also have abnormalities in congestive heart failure. Therefore, in these patients long-term oral ISDN therapy is given at a daily dose of 10 mg in divided doses.⁶

ISDN 5 mg tablets per 12 hours is a group of nitrates commonly used in patients with complaints of angina. In this patient, a picture of unifocal PVC and lead V2-V4 T wave inversion was found which showed the presence of coronary heart disease. In addition, patients also have congestive heart failure. Therefore, in this patient, long-term oral ISDN therapy was given at a daily dose of 10 mg in divided doses.¹³

One ampule of Ranitidine injection per 12 hours intravenously and 1 tablespoon of Antacids Syrup every 8 hours is the initial therapy for patients with suspected dyspepsia syndrome. In addition, this class of drugs also functions as an adjuvant drug in patients taking thromboaspilet drugs. The use of this drug was stopped after 1 week of patients' dyspepsia complaints improved.¹

Ubidecarenone and bisacodyl tablets were given as adjunctive drugs on the 6th-day care while coronary artery disease appeared on ECG finding. Ubideceranone functions as an antioxidant. In recent study, the use of antioxidant have a potential benefit in prevention of the coronary artery disease.¹⁴ Bisacodyl is a laxative agent that is intended to help reduce heart burden in patients, because it can reduce constipation-induced pressor effects as triggers for cardiovascular events.¹⁵

This patient was treated for 8 days in ICU, followed by 2 days in ward with good outcome. Early detection and intervention followed by close monitoring is a key

management for patient with hyperthyroid heart disease, especially in male patient, to achieve better outcome although in hospital with lack of resources. Limitations in this case report are that the thyroid function (TSH and fT_3/fT_4) and echocardiography were not assessed because the lack of resources in marginal region.

Conflict of Interest

There is no conflict of interest in publishing this article.

Funding Sources

There is no funding source in publishing this article.

Acknowledgments

The authors would like to thank dr. Nur Albar, Sp.PD, FINASIM as our supervisor during management of the patient.

References

1. Klein, I. & Danzi, S. Cardiovascular Involvement in General Medical Conditions Thyroid Disease and the Heart. (2015). doi:10.1161/CIRCULATIONAHA.106.678326
2. Siu, C., Yeung, C., Lau, C., Kung, A. W. C. & Tse, H. Incidence, clinical characteristics and outcome of congestive heart failure as the initial presentation in patients with primary hyperthyroidism. 483–487 (2007). doi:10.1136/hrt.2006.100628
3. D, A. & Y, K. Thyroid Heart Disease. in *Textbook on Internal Medicine Volume II* (eds. AW, S., B, S. & Alwi) 1798–1803 (Interna Publishing, 2009).
4. MM, P. Hypertention Heart Disease. in *Internal medicine textbook* (eds. AW, S., C, S. & Alwi) 1693 (Center for Publishing the Department of Internal Medicine FK UI, 2006).
5. DS, C., FS, G. & PW, L. The Thyroid Gland. in *Greenspan's Basic & Clinical Endocrinology* (eds. DG, G. & D, S.) (: The McGraw-Hill Companies, Inc, 2007).
6. BB, S., S, D., DA, J. & R, S. *Guidelines for the management of cardiovascular disease in Indonesia*. (Indonesian Association of Cardiovascular Specialists, 2009).
7. Chaudhry, L. ali, Mazen, K. F., Ba-Essa, E. & Robert, A. A. Case report Antithyroid drug induced agranulocytosis : what still we need to learn ? **8688**, 1–6 (2016).
8. Rizos, C. V, Elisaf, M. S. & Liberopoulos, E. N. Effects of Thyroid Dysfunction on Lipid Profile. 76–84 (2011).
9. Goldman, S. Thyroid and Cardiovascular Disease. 2892–2909 (2019). doi:10.1161/CIRCULATIONAHA.118.036859
10. Sklyar, E. *et al.* World Journal of Cardiology. **9**, 248–254 (2017).
11. A, G. *Introduction to the diagnosis of echocardiography*. (Department of Internal Medicine Science FKUI, 2009).
12. TF, D. Thyrotoxicosis. in (ed. HM, K.) (William Textbook of Endocrinology, 2008).
13. A, S. & Nafrialdi. *Medication for Heart Failure*. (Department of Pharmacology and Therapeutic FKUI, 2007).



14. A, J. & LD, L. Antioxidants and coronary artery disease: from athophysiology to preventive therapy. *Coron Artery Dis* **26**, 176–183 (2016).
15. Ishiyama, Y., Hoshide, S., Mizuno, H. & Kario, K. Constipation - induced pressor effects as triggers for cardiovascular events. *J Clin Hpertens* 1–5 (2019). doi:10.1111/jch.13489

Figure/Table

Table 1. Serial ECG during the patient follow up

Day of Care & Date	ECG Finding
Day-2 18/3/2016	<ul style="list-style-type: none"> • Atrial Fibrillation Normo Ventricular Response (NVR) HR 100x/minutes • Left Ventricular Hypertrophy (LVH) • Normoaxis
Day-6 22/3/2016	<ul style="list-style-type: none"> • Atrial Fibrillation Normo Ventricular Response (NVR) HR 90x/minutes • Left Ventricular Hypertrophy(LVH) • Normoaxis • T-Inverted V4-V6 suggestive Iskemik Anterolateral
Day-8 24/3/2016	<ul style="list-style-type: none"> • Atrial Fibrillation Normo Ventricular Response (NVR) HR 100x/minutes • Left Ventricular Hypertrophy(LVH) • Normoaxis • T-Inverted V4-V6 suggestive Iskemik Anterolateral • PVC/VES Unifocal
Day-9 25/3/2016	<ul style="list-style-type: none"> • Atrial Fibrillation Normo Ventricular Response (NVR) HR 80x/minutes • Left Ventricular Hypertrophy(LVH) • Normoaxis • T-Inverted V4-V6 suggestive Iskemik Anterolateral

Table 2. Resume of the follow-up during treatment in the ICU

Day of Care & Date	Assessment	Planning	Action*
Day-0 18/03 2016	<ul style="list-style-type: none"> • Palpitation • Hyperthyroid on treatment (PTU) • Trombocytopenia 	<ul style="list-style-type: none"> • Check the liver function, renal function, lipid profile, and electrolyte serum. • Observation for the vital sign q 4 hours • Perform serial ECG 	<ul style="list-style-type: none"> - O2 Nasal Canula 2 lpm - IVFD RL 20 dpm - Injection Ranitidin 1 amp/12 hours/ IV - Propanolol 20 mg/8 hours/PO - Bisoprolol 2,5 mg/24 hours/PO - PTU 100 mg/8 hours/PO
Day-1 19/03 2016	<ul style="list-style-type: none"> • Atrial Fibrillation • Congestive Heart Failiure • Hyperthyroid on treatment (PTU) • Trombocytopenia • Electrolyte imbalance 	<ul style="list-style-type: none"> • Check for the routine hematology 	<ul style="list-style-type: none"> - IVFD RL 18 dpm - Antacida syrup 10 ml/8 hours/PO
Day-2 20/03 2016	<ul style="list-style-type: none"> • Atrial Fibrillation • Congestive Heart Failure • Hyperthyroid on treatment (PTU) • Trombocytopenia • Electrolyte imbalance • Dyspepsia Syndrome 	<ul style="list-style-type: none"> • Check for the routine hematology 	<ul style="list-style-type: none"> - Antacida syrup 15 ml/8 hours/PO
Day-	<ul style="list-style-type: none"> • CHF e.c. Hyperthyroid 	<ul style="list-style-type: none"> • Check for the albumin and 	<ul style="list-style-type: none"> - Spironolactone 50 mg/8



3 21/03 2016	Heart Disease • Atrial Fibrillation • Hyperthyroid on treatment (PTU) • Trombocytopenia • Electrolyte imbalance • Dyspepsia Syndrome • Ascites e.c. CHF dd/ hypoproteinemia and hypoalbuminemia	protein total serum • Check for routine urinalysis • Perform chest X-Ray • Perform abdominal USG	<i>hours/PO</i>
Day- 4 22/03 2016	• CHF e.c. Hyperthyroid Heart Disease • Atrial Fibrillation • Hyperthyroid on treatment (PTU) • Trombocytopenia • Electrolyte imbalance • Dyspepsia Syndrome • Ascites e.c. CHF dd/ hypoproteinemia and hypoalbuminemia	• Check for the electrolyte serum	- <i>Injection Furosemide 20 mg/12 hours/IV</i>
Day- 5 23/03 2016	• CHF e.c. Hyperthyroid Heart Disease • Atrial Fibrillation • Hyperthyroid on treatment (PTU) • Trombocytopenia • Electrolyte imbalance • Dyspepsia Syndrome • Hypoproteinemia and hypoalbuminemia		- <i>Propranolol stop</i> - <i>High protein diet</i>
Day- 6 24/03 2016	• CHF e.c. Hyperthyroid Heart Disease • Atrial Fibrillation • Hyperthyroid on treatment (PTU) • Trombocytopenia • Dyspepsia Syndrome • Hypoproteinemia and hypoalbuminemia • Electrolyte Imbalance • Coronary Heart Disease	• Check albumin serum	- <i>Aff Oxygen Nasal Canule</i> - <i>Stop Injection Ranitidin and Furosemide</i> - <i>Furosemide 10 mg tab/24 hours/PO</i> - <i>Spirolactone 25 mg tab/24 hours/PO</i> - <i>Isosorbid Dinytrate 5 mg tab/12 hours/PO</i> - <i>Ubidecarenone 1 tablet/24 hours/PO</i> - <i>Bisacodyl 2 tablet every night</i> - <i>Digoxin 0,125 mg tab/ 12 hours/ PO</i> - <i>Thromboaspilet 1 tab/24 hours/PO</i>
Day- 7 25/03 2016	• CHF e.c. Hyperthyroid Heart Disease • Atrial Fibrillation • Hyperthyroid on treatment (PTU) • Trombocytopenia • Dyspepsia Syndrome • Hypoproteinemia and hypoalbuminemia		

- Electrolyte Imbalance
- Coronary Heart Disease

**Day-
8
26/03
2016**

- CHF e.c. Hyperthyroid Heart Disease
- Aarytmia
- Hyperthyroid on treatment (PTU)
- Trombocytopenia
- Dyspepsia Syndrome
- Hypoproteinemia and hypoalbuminemia
- Electrolyte Imbalance
- Coronary Heart Disease

- *Digoxin 0,125 mg tab/24 hours/PO*
- *Move into ward*

* Writing for the same action is not repeated.

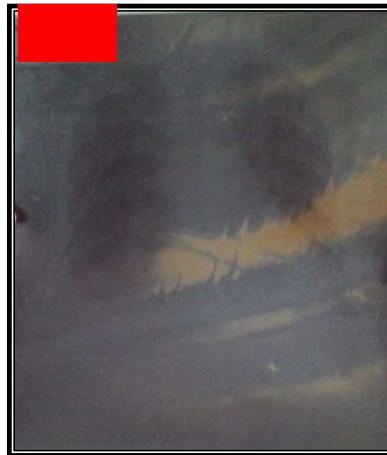


Figure 1. Radiologic Examination On 6th-Day Care